

**DOCKET NO.: ISIS0170-100 (ISPH-0524)****PATENT****REMARKS**

Claims 34-63 were pending. Upon entry of this amendment, claims 34-49, 51 and 53-63 will be pending. Claims 34, 36, 51, 59 and 63 are amended herein. Claims 50 and 52 are canceled as being redundant over amended claims 34 and 51. Claim 51 is amended to depend from claim 34 and to incorporate the 2'-sugar modifications specified therein. No new matter has been added to the claims. The claim amendments and cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action. Applicant reserves the right to file subsequent applications claiming the canceled subject matter.

**REJECTIONS UNDER 35 U.S.C. § 103**

Claims 34, 35, 38-40, 43-45 and 63 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cantin *et al.* (U.S. Patent No. 5,110,802). The Office Action asserts that Cantin *et al.* disclose an antisense oligonucleotide comprising oligoribonucleoside methylphosphonates, which is complementary to the first splice acceptor site of the tat III gene and blocks splicing of the RNA product of the tat III gene. The Office Action further states that it would have been obvious to one of skill in the art to modify the teachings of Cantin *et al.* to design methylphosphonate oligonucleotides targeting a wild-type cellular mRNA.

Without agreeing with the Examiner's position, and solely to advance prosecution of the instant application, Applicants have amended claim 34 to remove 3'-methylene phosphonate from the list of antisense compound modifications. As amended, claim 34, and all claims dependent therefrom, specify that the antisense compound has at least one modification selected from 2'-guanidinium, 2'-carbamate and 2'-aminoxy. Since Cantin *et al.* do not teach or suggest 2'-guanidinium, 2'-carbamate or 2'-aminoxy modifications, nor any sugar modifications, the cited reference does not teach or suggest all of the claim limitations.

Accordingly, Applicants respectfully submit that the current claims are not *prima facie* obvious and request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

**DOCKET NO.: ISIS0170-100 (ISPH-0524)****PATENT****REJECTIONS UNDER 35 U.S.C. § 112**

Claims 36, 52, 59 and 63 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. The Examiner states that in claims 36 and 52, "2'-acetamino" and "2'-dimethylaminoethoxyethoxy" lack antecedent basis. Claim 36 is amended to remove 2'-acetamino and 2'-dimethylaminoethoxyethoxy and claim 52 is canceled herein, thus rendering this rejection moot.

The Examiner states that claim 59 is indefinite because "said modified nucleobase is a C-5 propyne" lacks antecedent basis. Applicants have amended claim 59 to depend from claim 58, which introduces antisense compounds comprising at least one modified nucleobase.

The Office Action also points out a grammatical error in claim 63, which Applicants have corrected herein by amending claim 63 to include the preposition "at."

**Claims 34-63** are rejected under 35 U.S.C. § 112, first paragraph. The Office Action states that while the specification provides enablement for practicing the claimed invention *in vitro*, it does not reasonably provide enablement for practicing the claimed invention *in vivo* for therapeutic treatment (page 4 of the Office Action dated March 31, 2004).

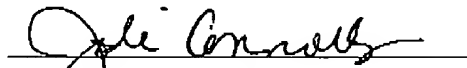
Without responding to the merits of this rejection, and solely to advance prosecution of the instant application, Applicants have amended claim 34 to specify that the method comprises binding an antisense compound to a wild-type cellular mRNA target *in vitro*. Since claims 35-63 all depend from claim 34, either directly or indirectly, all pending claims now specify an *in vitro* method. Applicants reserve the right to file subsequent applications claiming the cancelled subject matter. In addition, the claim amendments should not be construed as abandonment or agreement with the Examiner's position in the Office Action. Applicants respectfully request reconsideration and withdrawal of these grounds for rejection.

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It is believed that no fee is due with this response. However, if a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 50-0252.

Withdrawal of the pending rejections and reconsideration of the claims is respectfully requested.

Respectfully submitted,



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